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# LETTERS AND CORRESPONDENCE

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## Hunter's Syndrome With an Endogenous Anticoagulant

*To the Editor:* I read with interest the article of Billett et al. [1] describing coagulation abnormalities in Gaucher's disease. A different mechanism is proposed for the presence of an endogenous anticoagulant complicating Hunter's syndrome in an adult, the neurologic features of which have recently been described [2].

The anticoagulant was detected while investigating the cause of an unexpected extradural hemorrhage following ventriculoperitoneal shunt insertion. The patient had no previous bleeding history with minor orthopedic procedures. He had hepatosplenomegaly and intermittent thrombocytopenia (platelets, 80–150 $\times$ $10^9$/l), thought to be secondary to mucopolysaccharide deposition.

His activated partial thromboplastin time (APTT) was persistently prolonged to 43 sec (normal, 25–35 sec), which was corrected with the addition of normal plasma. He had a normal thrombin clotting time (TCT), excluding heparin and anti-IIa activity. Factor VIII, IX, XI, and XII levels were normal. Lupus anticoagulant studies were negative. Heparin cofactor II activity (Stago, Asnières, France) was decreased, to 57% (normal, 65–145%). Antithrombin III (ATIII) activity (Organon Teknika, Durham, NC) was also decreased, to 64% activity (normal, 83–131%), and an anti-Xa assay using danaparoid sodium as comparitor showed activity at 0.04 U/ml. D-dimer levels (Agen, Brisbane, Queensland, Australia) were <0.25 mg/ml. Testing for heparinoid-dependent platelet aggregation was negative. Urinary glycosaminoglycans (predominantly heparan and dermatan sulphate) were 390 mg/g creatinine (normal, ≤180 mg/g).

The occurrence of surgical bleeding does not correlate well with the plasma anti-Xa level within therapeutic range. It was very low in our patient, and his thrombocytopenia was likely additive to his bleeding risk.

The low ATIII and heparin cofactor II levels most probably reflect increased clearance of ATIII-thrombin-heparan sulfate, heparan cofactor II-thrombin-heparan sulfate, or heparin cofactor II-dermatan sulfate complexes with thrombin, generated analagous to the reduced ATIII levels seen after heparin administration.

Hunter's syndrome is a class II mucopolysaccharidosis, an X-linked condition caused by iduronate-2-sulphatase deficiency [3]. This enzyme degrades heparan sulfate and dermatan sulfate, and its deficiency results in accumulation of these mucopolysaccharides throughout the body, with increased urinary excretion. Heparan sulfate binds to plasma ATIII to rapidly inhibit thrombin, factor Xa, and factor IXa. Heparan sulfate and dermatan sulfate bind to heparin cofactor II to increase the rate of inhibition of thrombin by 1,000-fold [4]. These properties are exploited in the therapeutic applications of the heparinoid danaparoid sodium, a mixture of heparan (HS), dermatan (DS), and chondriotin sulfate (CS), used for thromboprophylaxis and in patients with noncrossreacting heparin-associated thrombocytopenia. The anti-Xa:anti-IIa activities are 20:1, and these compounds have little effect on platelet function compared with heparin [5]. Our patient's plasma showed anti-Xa activity only, which was at low levels and not unexpectedly corrected by the in vitro addition of normal plasma. This level would not be expected to prolong the APTT, which remains unexplained, but is similar to levels seen in "prophylactic" dosage treatment.

It is unclear from the literature whether patients with mucopolysaccharidoses, nearly all of whom have high levels of HS and/or DS, have risks which are increased for surgical bleeding and/or more possibly reduced for thrombotic events, which might be anticipated from their autoanticoagulation.

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### References

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5. Meuleman DG, Hobbelen PMJ, van Dedem G, Moelker HCT: A novel antithrombotic heparinoid (ORG 10172) devoid of bleeding inducing capacity. A survey of its pharmacological properties in experimental animal models. Thromb Res 27:353–363, 1982.

## BCR-ABL Rearrangement in Adult T-Cell Acute Lymphoblastic Leukemia

*To the Editor:* Approximately 30% of adult acute lymphoblastic leukemia (ALL) cases, mostly of B lineage, contain the BCR-ABL fusion gene [1–4]. Most commonly, BCR-ABL results from a reciprocal translocation between chromosomes 9 and 22, generating the classic Philadelphia (Ph) chromosome [5]. In the remaining cases, a complex translocation involving a third chromosome masks the Ph marker [6], or else the fusion gene is created by the insertion of ABL sequences into the BCR gene of a normal-appearing chromosome 22. Cytogenetic analysis generally detects at least 50% of